

(19)



Europäisches Patentamt  
European Patent Office  
Office européen des brevets



(11)

**EP 0 974 600 A3**

(12)

**EUROPEAN PATENT APPLICATION**

(88) Date of publication A3:  
19.09.2001 Bulletin 2001/38

(51) Int Cl.7: **C07K 16/24**, C12N 15/13,  
A61K 39/395

(43) Date of publication A2:  
26.01.2000 Bulletin 2000/04

(21) Application number: **99304977.4**

(22) Date of filing: **24.06.1999**

(84) Designated Contracting States:  
**AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU  
MC NL PT SE**  
Designated Extension States:  
**AL LT LV MK RO SI**

(30) Priority: **24.06.1998 JP 17758098**  
**12.10.1998 JP 28904498**  
**22.12.1998 JP 36502398**

(71) Applicant: **KABUSHIKI KAISHA HAYASHIBARA  
SEIBUTSU KAGAKU KENKYUJO**  
**Okayama-shi Okayama (JP)**

(72) Inventors:  
• **Nishida, Yoshihiro**  
**Okayama (JP)**  
• **Okura, Takanori**  
**Kurashiki-shi, Okayama (JP)**  
• **Tanimoto, Tadao**  
**Okayama-shi, Okayama (JP)**  
• **Kurimoto, Masashi**  
**Okayama-shi, Okayama (JP)**

(74) Representative: **Daniels, Jeffrey Nicholas et al**  
**Page White & Farrer**  
**54 Doughty Street**  
**London WC1N 2LS (GB)**

(54) **Anti-interleukin-18 antibody**

(57) Disclosed are artificially produced peptide capable of neutralizing the biological activities of IL-18, which comprises a part or the whole of the variable regions in anti-interleukin-18 antibody, including single chain variable region fragments and humanized anti-

bodies, a process of producing the peptide, and uses thereof. The peptide is useful as pharmaceutical to treat and prevent diseases such as autoimmune diseases and inflammatory diseases, where the biological activities of interleukin-18 are involved.

**EP 0 974 600 A3**



European Patent  
Office

# PARTIAL EUROPEAN SEARCH REPORT

Application Number

which under Rule 45 of the European Patent Convention shall be considered, for the purposes of subsequent proceedings, as the European search report

EP 99 30 4977

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
X	WO 97 44468 A (SCHERING CORP) 27 November 1997 (1997-11-27)	1-7, 9-12, 14-27	C07K16/24 C12N15/13 A61K39/395
Y	* page 3, line 10 - page 3, line 37 * * page 4, line 9 - page 4, line 21 * * page 5, line 21 - page 5, line 25 * * page 6, line 4 - page 6, line 21 * * page 7, line 8 - page 7, line 13 * * page 11, line 10 - page 11, line 18 * * page 23, line 24 - page 25, line 3 * * page 32, line 4 - page 35, line 28 * * page 40, line 13 - page 41, line 15 * * page 47 * * claims 1-6 *  ---  -/--	8,13	
			TECHNICAL FIELDS SEARCHED (Int.Cl.6)
			C07K C12N A61K
INCOMPLETE SEARCH			
<p>The Search Division considers that the present application, or one or more of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for these claims.</p> <p>Claims searched completely :</p> <p>Claims searched incompletely :</p> <p>Claims not searched :</p> <p>Reason for the limitation of the search:</p> <p>Although claims 25 and 27 are directed to a method of treatment of the human/animal body (Article 52(4) EPC), the search has been carried out and based on the alleged effects of the compound/composition.</p>			
Place of search		Date of completion of the search	Examiner
MUNICH		26 July 2001	Renggli, J
CATEGORY OF CITED DOCUMENTS			
<p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons &amp; : member of the same patent family, corresponding document</p>			

EPO FORM 1503 03.82 (P04007)



European Patent  
Office

## PARTIAL EUROPEAN SEARCH REPORT

Application Number  
EP 99 30 4977

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	TANIGUCHI M ET AL: "Characterization of anti-human interleukin-18 (IL-18)/interferon-gamma-inducing factor (IGIF) monoclonal antibodies and their application in the measurement of human IL-18 by ELISA" JOURNAL OF IMMUNOLOGICAL METHODS, ELSEVIER SCIENCE PUBLISHERS B.V., AMSTERDAM, NL, vol. 206, no. 1-2, 7 August 1997 (1997-08-07), pages 107-113, XP004093123 ISSN: 0022-1759	1-7, 9-12, 14-27	
Y	* the whole document * ---	8,13	
X	H TSUTSUI ET AL: "IL-18 accounts for both TNF-alpha- and Fas ligand-mediated hepatotoxic pathways in endotoxin-induced liver injury in mice" JOURNAL OF IMMUNOLOGY, US, THE WILLIAMS AND WILKINS CO. BALTIMORE, vol. 159, no. 8, 15 October 1997 (1997-10-15), pages 3961-3967, XP002141329 ISSN: 0022-1767	1-7, 9-12, 14-27	TECHNICAL FIELDS SEARCHED (Int.Cl.6)
Y	* the whole document * ---	8,13	
A	DINARELLO C A ET AL: "OVERVIEW OF INTERLEUKIN-18: MORE THEN AN INTERFERON-GAMMA INDUCING FACTOR" JOURNAL OF LEUKOCYTE BIOLOGY, FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL, US, vol. 63, no. 6, 1 June 1998 (1998-06-01), pages 658-664, XP000973451 ISSN: 0741-5400 * the whole document * ---	1-27	
	-/--		

EPO FORM 1503 03.02 (P04C10)



European Patent  
Office

## PARTIAL EUROPEAN SEARCH REPORT

Application Number  
EP 99 30 4977

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
P, X	EP 0 850 952 A (HAYASHIBARA BIOCHEM LAB) 1 July 1998 (1998-07-01)  * page 5, line 29 - page 6, line 53; claims 1-28 * * page 7, line 23 - page 7, line 34 * * page 11 - page 12 *	1-7, 9-12, 14-27	
P, X	WO 99 09063 A (RUBINSTEIN MENACHEM ;KIM SOO HYUN (IL); NOVICK DANIELA (IL); YEDA) 25 February 1999 (1999-02-25) * claims 1-25,32-41; examples 5,7,9,17 *	1-7, 9-12, 14-27	
E	WO 01 45747 A (TECHNION RES & DEV FOUNDATION ;WILDBAUM GIZI (IL); CARIN NATHAN (I) 28 June 2001 (2001-06-28) * page 20 - page 24; claims 1-5,8-11 * * page 10 *	1-7, 9-12, 14-27	TECHNICAL FIELDS SEARCHED (Int.Cl.6)
E	WO 00 56771 A (HOLMES STEPHEN D ;SMITHKLINE BEECHAM PLC (GB); ABDEL MEGUID SHERIN) 28 September 2000 (2000-09-28) * page 10 - page 26; claims 1-24; figures 1-6 *	1-7, 9-12, 14-27	

**ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.**

EP 99 30 4977

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on  
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

26-07-2001

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9744468	A	27-11-1997	AU 3116697 A	09-12-1997
			EP 0914453 A	12-05-1999
			JP 2000511418 T	05-09-2000
EP 0850952	A	01-07-1998	AU 4922497 A	02-07-1998
			CA 2219963 A	26-06-1998
			JP 11100400 A	13-04-1999
WO 9909063	A	25-02-1999	AU 8746098 A	08-03-1999
			BG 104149 A	31-08-2000
			BR 9811940 A	05-09-2000
			CN 1267307 T	20-09-2000
			DE 1003781 T	11-01-2001
			EE 200000073 A	16-10-2000
			EP 1003781 A	31-05-2000
			ES 2149149 T	01-11-2000
			HU 0003533 A	29-01-2001
			NO 20000700 A	14-04-2000
			PL 338647 A	06-11-2000
			SK 1762000 A	12-09-2000
WO 0145747	A	28-06-2001	NONE	
WO 0056771	A	28-09-2000	NONE	

EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82